



SEQUENCE LISTING

<110> Vanderbilt University
 Balser, Jeffrey
 George, Alfred
 Roden, Dan

<120> HUMAN KCR1 REGULATION OF HERG POTASSIUM CHANNEL BLOCK

<130> 1242-49-2

<140> US/10/000,151

<141> 2001-10-30

<150> 60/244,340

<151> 2000-10-30

<160> 7

<170> PatentIn version 3.0

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<211> 1857

<212> DNA

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15

ttt tta gtg tcc tgc ctc ctc ttc tcc gcc ttc agc cgg gcg ctg cga
 96

Phe Leu Val Ser Cys Leu Leu Phe Ser Ala Phe Ser Arg Ala Leu Arg

20

25

30

gag ccc tac atg gac gag atc ttc cac ctg cct cag gcg cag cgc tac

144
 Glu Pro Tyr Met Asp Glu Ile Phe His Leu Pro Gln Ala Gln Arg Tyr
 35 40 45
 tgt gag ggc cat ttc tcc ctt tcc cag tgg gat ccc atg att act aca
 192
 Cys Glu Gly His Phe Ser Leu Ser Gln Trp Asp Pro Met Ile Thr Thr
 50 55 60
 tta cct ggc ttg tac ctg gtg tca gtt gga gtg gtc aaa cct gcc att
 240
 Leu Pro Gly Leu Tyr Leu Val Ser Val Gly Val Val Lys Pro Ala Ile
 65 70 75 80
 tgg atc ttt gga tgg tct gaa cat gtt gtc tgc tcc att ggg atg ctc
 288
 Trp Ile Phe Gly Trp Ser Glu His Val Val Cys Ser Ile Gly Met Leu
 85 90 95
 aga ttt gtt aat ctt ctc ttc agt gtt ggc aac ttc tat tta cta tat
 336
 Arg Phe Val Asn Leu Leu Phe Ser Val Gly Asn Phe Tyr Leu Leu Tyr
 100 105 110
 ttg ctt ttc cac aag gta caa ccc aga aac aag gct gcc tca agt atc
 384
 Leu Leu Phe His Lys Val Gln Pro Arg Asn Lys Ala Ala Ser Ser Ile
 115 120 125
 cag aga gtc ttg tca aca tta aca cta gca gta ttt cca aca ctt tat
 432
 Gln Arg Val Leu Ser Thr Leu Thr Leu Ala Val Phe Pro Thr Leu Tyr
 130 135 140

ttt ttt aac ttc ctt tat tat aca gaa gca gga tct atg ttt ttt act
480

Phe Phe Asn Phe Leu Tyr Tyr Thr Glu Ala Gly Ser Met Phe Phe Thr

145 150 155 160

ctt ttt gca tat ttg atg tgt ctt tat gga aat cat aaa act tca gcc
528

Leu Phe Ala Tyr Leu Met Cys Leu Tyr Gly Asn His Lys Thr Ser Ala

165 170 175

ttc ctt gga ttt tgt ggc ttc atg ttt cgg caa aca aat atc atc tgg
576

Phe Leu Gly Phe Cys Gly Phe Met Phe Arg Gln Thr Asn Ile Ile Trp

180 185 190

gct gtc ttc tgt gca ggg aat gtc att gca caa aag tta act gag gct
624

Ala Val Phe Cys Ala Gly Asn Val Ile Ala Gln Lys Leu Thr Glu Ala

195 200 205

tgg aaa act gag cta caa aag aag gaa gac aga ctt cca cct att aaa
672

Trp Lys Thr Glu Leu Gln Lys Lys Glu Asp Arg Leu Pro Pro Ile Lys

210 215 220

gga cca ttt gca gaa ttc aga aaa att ctt cag ttt ctt ttg gct tat
720

Gly Pro Phe Ala Glu Phe Arg Lys Ile Leu Gln Phe Leu Leu Ala Tyr

225 230 235 240

tcc atg tcc ttt aaa aac ttg agt atg ctt ttc tgt ttg act tgg ccc
768

Ser Met Ser Phe Lys Asn Leu Ser Met Leu Phe Cys Leu Thr Trp Pro

245 250 255

tac atc ctt ctg gga ttt ctg ttt tgt gct ttt gta gta gtt aat ggt
816

Tyr Ile Leu Leu Gly Phe Leu Phe Cys Ala Phe Val Val Val Asn Gly

260

265

270

gga att gtt att ggc gat cgg agt agt cat gaa gcc tgt ctt cat ttt
864

Gly Ile Val Ile Gly Asp Arg Ser Ser His Glu Ala Cys Leu His Phe

275

280

285

cct caa cta ttc tac ttt ttt tca ttt act ctc ttt ttt tct ttt cct
912

Pro Gln Leu Phe Tyr Phe Phe Ser Phe Thr Leu Phe Phe Ser Phe Pro

290

295

300

cat ctc ctg tct cct agc aaa att aag act ttt ctt tcc tta gtt tgg
960

His Leu Leu Ser Pro Ser Lys Ile Lys Thr Phe Leu Ser Leu Val Trp

305

310

315

320

aaa cat gga att ctg ttt ttg gtg gtt acc tta gtc tct gtg ttt tta
1008

Lys His Gly Ile Leu Phe Leu Val Val Thr Leu Val Ser Val Phe Leu

325

330

335

gtt tgg aaa ttc act tat gct cat aaa tac ttg cta gca gac aat aga
1056

Val Trp Lys Phe Thr Tyr Ala His Lys Tyr Leu Leu Ala Asp Asn Arg

340

345

350

cat tat act ttc tat gtg tgg aaa aga gtt ttt caa aga tat gca att
1104

His Tyr Thr Phe Tyr Val Trp Lys Arg Val Phe Gln Arg Tyr Ala Ile

355

360

365

ctg aaa tat ttg tta gtt cca gcc tat ata ttt gct ggt tgg agt ata
1152

Leu Lys Tyr Leu Leu Val Pro Ala Tyr Ile Phe Ala Gly Trp Ser Ile

370

375

380

gct gac tca ttg aaa tca aag cca att ttt tgg aat tta atg ttt ttc
1200

Ala Asp Ser Leu Lys Ser Lys Pro Ile Phe Trp Asn Leu Met Phe Phe

385

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395

400

ata tgc ttg ttc att gtt ata gtt cct cag aaa ctg ctg gaa ttt cgt
1248

Ile Cys Leu Phe Ile Val Ile Val Pro Gln Lys Leu Leu Glu Phe Arg

405

410

415

tac ttc att tta cct tat gtc att tat agg ctt aac ata act ctg cct
1296

Tyr Phe Ile Leu Pro Tyr Val Ile Tyr Arg Leu Asn Ile Thr Leu Pro

420

425

430

ccc aca tcc aga ctt gtt tgt gaa ctg agt tgc tat gca att gtt aat
1344

Pro Thr Ser Arg Leu Val Cys Glu Leu Ser Cys Tyr Ala Ile Val Asn

435

440

445

ttc ata act ttt tac atc ttt ctg aac aag act ttt cag tgg cca aat
1392

Phe Ile Thr Phe Tyr Ile Phe Leu Asn Lys Thr Phe Gln Trp Pro Asn

450

455

460

agt cag gac att caa agg ttt atg tgg taa tatcagtgat attttgaact
1442

Ser Gln Asp Ile Gln Arg Phe Met Trp

465

470

gtaaaaatgg acttaataat agaccatttc tacaaagaac aactgaatag gnggaaaaca
1502

tggaatttct tttaggtgca gtggtggtct tcaaattaca ttagtttttt taatatatat
1562

tttaaacata tgtaagaaat taagtggcaa agaactggga aagcttaaga cctgcttcaa
1622

angcctgaat aatgggaaaa taaanwngtt tncagatatc tcatatcgct cnnknatgn
1682

tggcccytmn caangcttgg gaatgkttnn wntgnataag ttnattaaan ctgggnntgc
1742

tnnmwatnac ttnnkncca nccwnnnwac natgnnntan nnantattta caaaggtcag
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<213> Homo sapiens

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Glu	Pro	Tyr	Met	Asp	Glu	Ile	Phe	His	Leu	Pro	Gln	Ala	Gln	Arg	Tyr
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Cys	Glu	Gly	His	Phe	Ser	Leu	Ser	Gln	Trp	Asp	Pro	Met	Ile	Thr	Thr
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Leu Pro Gly Leu Tyr Leu Val Ser Val Gly Val Val Lys Pro Ala Ile
 65 70 75 80

Trp Ile Phe Gly Trp Ser Glu His Val Val Cys Ser Ile Gly Met Leu
 85 90 95

Arg Phe Val Asn Leu Leu Phe Ser Val Gly Asn Phe Tyr Leu Leu Tyr
 100 105 110

Leu Leu Phe His Lys Val Gln Pro Arg Asn Lys Ala Ala Ser Ser Ile
 115 120 125

Gln Arg Val Leu Ser Thr Leu Thr Leu Ala Val Phe Pro Thr Leu Tyr
 130 135 140

Phe Phe Asn Phe Leu Tyr Tyr Thr Glu Ala Gly Ser Met Phe Phe Thr
 145 150 155 160

Leu Phe Ala Tyr Leu Met Cys Leu Tyr Gly Asn His Lys Thr Ser Ala
 165 170 175

Phe Leu Gly Phe Cys Gly Phe Met Phe Arg Gln Thr Asn Ile Ile Trp
 180 185 190

Ala Val Phe Cys Ala Gly Asn Val Ile Ala Gln Lys Leu Thr Glu Ala
 195 200 205

Trp Lys Thr Glu Leu Gln Lys Lys Glu Asp Arg Leu Pro Pro Ile Lys
 210 215 220

Gly Pro Phe Ala Glu Phe Arg Lys Ile Leu Gln Phe Leu Leu Ala Tyr
 225 230 235 240

Ser Met Ser Phe Lys Asn Leu Ser Met Leu Phe Cys Leu Thr Trp Pro
 245 250 255

Tyr Ile Leu Leu Gly Phe Leu Phe Cys Ala Phe Val Val Val Asn Gly
 260 265 270

Gly Ile Val Ile Gly Asp Arg Ser Ser His Glu Ala Cys Leu His Phe
 275 280 285

Pro Gln Leu Phe Tyr Phe Phe Ser Phe Thr Leu Phe Phe Ser Phe Pro
 290 295 300

His Leu Leu Ser Pro Ser Lys Ile Lys Thr Phe Leu Ser Leu Val Trp
 305 310 315 320

Lys His Gly Ile Leu Phe Leu Val Val Thr Leu Val Ser Val Phe Leu
 325 330 335

Val Trp Lys Phe Thr Tyr Ala His Lys Tyr Leu Leu Ala Asp Asn Arg
 340 345 350

His Tyr Thr Phe Tyr Val Trp Lys Arg Val Phe Gln Arg Tyr Ala Ile
 355 360 365

Leu Lys Tyr Leu Leu Val Pro Ala Tyr Ile Phe Ala Gly Trp Ser Ile
 370 375 380

Ala Asp Ser Leu Lys Ser Lys Pro Ile Phe Trp Asn Leu Met Phe Phe
 385 390 395 400

Ile Cys Leu Phe Ile Val Ile Val Pro Gln Lys Leu Leu Glu Phe Arg
 405 410 415

Tyr Phe Ile Leu Pro Tyr Val Ile Tyr Arg Leu Asn Ile Thr Leu Pro
 420 425 430

Pro Thr Ser Arg Leu Val Cys Glu Leu Ser Cys Tyr Ala Ile Val Asn
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Asn Ala Arg Val Glu Asn Cys Ala Val Ile Tyr Cys Asn Asp Gly Phe
35 40 45

Cys Glu Leu Cys Gly Tyr Ser Arg Ala Glu Val Met Gln Arg Pro Cys
50 55 60

Thr Cys Asp Phe Leu His Gly Pro Arg Thr Gln Arg Arg Ala Ala Ala
65 70 75 80

Gln Ile Ala Gln Ala Leu Leu Gly Ala Glu Glu Arg Lys Val Glu Ile
85 90 95

Ala Phe Tyr Arg Lys Asp Gly Ser Cys Phe Leu Cys Leu Val Asp Val
100 105 110

Val Pro Val Lys Asn Glu Asp Gly Ala Val Ile Met Phe Ile Leu Asn
115 120 125

Phe Glu Val Val Met Glu Lys Asp Met Val Gly Ser Pro Ala His Asp
130 135 140

Thr Asn His Arg Gly Pro Pro Thr Ser Trp Leu Ala Pro Gly Arg Ala
145 150 155 160

Lys Thr Phe Arg Leu Lys Leu Pro Ala Leu Leu Ala Leu Thr Ala Arg
165 170 175

Glu	Ser	Ser	Val	Arg	Ser	Gly	Gly	Ala	Gly	Gly	Ala	Gly	Ala	Pro	Gly
			180					185					190		
Ala	Val	Val	Val	Asp	Val	Asp	Leu	Thr	Pro	Ala	Ala	Pro	Ser	Ser	Glu
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Ser	Leu	Ala	Leu	Asp	Glu	Val	Thr	Ala	Met	Asp	Asn	His	Val	Ala	Gly
	210					215					220				
Leu	Gly	Pro	Ala	Glu	Glu	Arg	Arg	Ala	Leu	Val	Gly	Pro	Gly	Ser	Pro
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Pro	Arg	Ser	Ala	Pro	Gly	Gln	Leu	Pro	Ser	Pro	Arg	Ala	His	Ser	Leu
				245					250					255	
Asn	Pro	Asp	Ala	Ser	Gly	Ser	Ser	Cys	Ser	Leu	Ala	Arg	Thr	Arg	Ser
			260					265					270		
Arg	Glu	Ser	Cys	Ala	Ser	Val	Arg	Arg	Ala	Ser	Ser	Ala	Asp	Asp	Ile
		275					280					285			
Glu	Ala	Met	Arg	Ala	Gly	Val	Leu	Pro	Pro	Pro	Pro	Arg	His	Ala	Ser
	290					295					300				
Thr	Gly	Ala	Met	His	Pro	Leu	Arg	Ser	Gly	Leu	Leu	Asn	Ser	Thr	Ser
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Asp	Ser	Asp	Leu	Val	Arg	Tyr	Arg	Thr	Ile	Ser	Lys	Ile	Pro	Gln	Ile
				325					330					335	
Thr	Leu	Asn	Phe	Val	Asp	Leu	Lys	Gly	Asp	Pro	Phe	Leu	Ala	Ser	Pro
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Thr	Ser	Asp	Arg	Glu	Ile	Ile	Ala	Pro	Lys	Ile	Lys	Glu	Arg	Thr	His
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Asn	Val	Thr	Glu	Lys	Val	Thr	Gln	Val	Leu	Ser	Leu	Gly	Ala	Asp	Val
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Leu	Pro	Glu	Tyr	Lys	Leu	Gln	Ala	Pro	Arg	Ile	His	Arg	Trp	Thr	Ile
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Leu	His	Tyr	Ser	Pro	Phe	Lys	Ala	Val	Trp	Asp	Trp	Leu	Ile	Leu	Leu
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Leu	Val	Ile	Tyr	Thr	Ala	Val	Phe	Thr	Pro	Tyr	Ser	Ala	Ala	Phe	Leu
			420					425					430		

Leu	Lys	Glu	Thr	Glu	Glu	Gly	Pro	Pro	Ala	Thr	Glu	Cys	Gly	Tyr	Ala		
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Cys	Gln	Pro	Leu	Ala	Val	Val	Asp	Leu	Ile	Val	Asp	Ile	Met	Phe	Ile		
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Val	Asp	Ile	Leu	Ile	Asn	Phe	Arg	Thr	Thr	Tyr	Val	Asn	Ala	Asn	Glu		
465					470					475					480		
Glu	Val	Val	Ser	His	Pro	Gly	Arg	Ile	Ala	Val	His	Tyr	Phe	Lys	Gly		
				485					490					495			
Trp	Phe	Leu	Ile	Asp	Met	Val	Ala	Ala	Ile	Pro	Phe	Asp	Leu	Leu	Ile		
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Phe	Gly	Ser	Gly	Ser	Glu	Glu	Leu	Ile	Gly	Leu	Leu	Lys	Thr	Ala	Arg		
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Leu	Leu	Arg	Leu	Val	Arg	Val	Ala	Arg	Lys	Leu	Asp	Arg	Tyr	Ser	Glu		
	530					535					540						
Tyr	Gly	Ala	Ala	Val	Leu	Phe	Leu	Leu	Met	Cys	Thr	Phe	Ala	Leu	Ile		
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Ala	His	Trp	Leu	Ala	Cys	Ile	Trp	Tyr	Ala	Ile	Gly	Asn	Met	Glu	Gln		
				565					570					575			
Pro	His	Met	Asp	Ser	Arg	Ile	Gly	Trp	Leu	His	Asn	Leu	Gly	Asp	Gln		
			580					585					590				
Ile	Gly	Lys	Pro	Tyr	Asn	Ser	Ser	Gly	Leu	Gly	Gly	Pro	Ser	Ile	Lys		
		595					600					605					
Asp	Lys	Tyr	Val	Thr	Ala	Leu	Tyr	Phe	Thr	Phe	Ser	Ser	Leu	Thr	Ser		
	610					615					620						
Val	Gly	Phe	Gly	Asn	Val	Ser	Pro	Asn	Thr	Asn	Ser	Glu	Lys	Ile	Phe		
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Ser	Ile	Cys	Val	Met	Leu	Ile	Gly	Ser	Leu	Met	Tyr	Ala	Ser	Ile	Phe		
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Gly	Asn	Val	Ser	Ala	Ile	Ile	Gln	Arg	Leu	Tyr	Ser	Gly	Thr	Ala	Arg		
			660					665					670				
Tyr	His	Thr	Gln	Met	Leu	Arg	Val	Arg	Glu	Phe	Ile	Arg	Phe	His	Gln		
		675					680					685					

Ile	Pro	Asn	Pro	Leu	Arg	Gln	Arg	Leu	Glu	Glu	Tyr	Phe	Gln	His	Ala	
	690					695					700					
Trp	Ser	Tyr	Thr	Asn	Gly	Ile	Asp	Met	Asn	Ala	Val	Leu	Lys	Gly	Phe	
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Pro	Glu	Cys	Leu	Gln	Ala	Asp	Ile	Cys	Leu	His	Leu	Asn	Arg	Ser	Leu	
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Leu	Gln	His	Cys	Lys	Pro	Phe	Arg	Gly	Ala	Thr	Lys	Gly	Cys	Leu	Arg	
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Ala	Leu	Ala	Met	Lys	Phe	Lys	Thr	Thr	His	Ala	Pro	Pro	Gly	Asp	Thr	
		755					760					765				
Leu	Val	His	Ala	Gly	Asp	Leu	Leu	Thr	Ala	Leu	Tyr	Phe	Ile	Ser	Arg	
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Gly	Ser	Ile	Glu	Ile	Leu	Arg	Gly	Asp	Val	Val	Val	Ala	Ile	Leu	Gly	
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Lys	Asn	Asp	Ile	Phe	Gly	Glu	Pro	Leu	Asn	Leu	Tyr	Ala	Arg	Pro	Gly	
				805					810					815		
Lys	Ser	Asn	Gly	Asp	Val	Arg	Ala	Leu	Thr	Tyr	Cys	Asp	Leu	His	Lys	
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Ile	His	Arg	Asp	Asp	Leu	Leu	Glu	Val	Leu	Asp	Met	Tyr	Pro	Glu	Phe	
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Ser	Asp	His	Phe	Trp	Ser	Ser	Leu	Glu	Ile	Thr	Phe	Asn	Leu	Arg	Asp	
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Thr	Asn	Met	Ile	Pro	Gly	Ser	Pro	Gly	Ser	Thr	Glu	Leu	Glu	Gly	Gly	
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Phe	Ser	Arg	Gln	Arg	Lys	Arg	Lys	Leu	Ser	Phe	Arg	Arg	Arg	Thr	Asp	
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Lys	Asp	Thr	Glu	Gln	Pro	Gly	Glu	Val	Ser	Ala	Leu	Gly	Pro	Gly	Arg	
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Ala	Gly	Ala	Gly	Pro	Ser	Ser	Arg	Gly	Arg	Pro	Gly	Gly	Pro	Trp	Gly	
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Glu	Ser	Pro	Ser	Ser	Gly	Pro	Ser	Ser	Pro	Glu	Ser	Ser	Glu	Asp	Glu	
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Gly Pro Gly Arg Ser Ser Ser Pro Leu Arg Leu Val Pro Phe Ser Ser
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Pro Arg Pro Pro Gly Glu Pro Pro Gly Gly Glu Pro Leu Met Glu Asp
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Cys Glu Lys Ser Ser Asp Thr Cys Asn Pro Leu Ser Gly Ala Phe Ser
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Gly Val Ser Asn Ile Phe Ser Phe Trp Gly Asp Ser Arg Gly Arg Gln
 995 1000 1005

Tyr Gln Glu Leu Pro Arg Cys Pro Ala Pro Thr Pro Ser Leu Leu
 1010 1015 1020

Asn Ile Pro Leu Ser Ser Pro Gly Arg Arg Pro Arg Gly Asp Val
 1025 1030 1035

Glu Ser Arg Leu Asp Ala Leu Gln Arg Gln Leu Asn Arg Leu Glu
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Thr Arg Leu Ser Ala Asp Met Ala Thr Val Leu Gln Leu Leu Gln
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Arg Gln Met Thr Leu Val Pro Pro Ala Tyr Ser Ala Val Thr Thr
 1070 1075 1080

Pro Gly Pro Gly Pro Thr Ser Thr Ser Pro Leu Leu Pro Val Ser
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Pro Leu Pro Thr Leu Thr Leu Asp Ser Leu Ser Gln Val Ser Gln
 1100 1105 1110

Phe Met Ala Cys Glu Glu Leu Pro Pro Gly Ala Pro Glu Leu Pro
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<213> Homo sapiens

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109

Met Ser Thr Leu Ser Asn Phe Thr Gln Thr Leu Glu

1

5

10

gac gtc ttc cga agg att ttt att act tat atg gac aat tgg cgc cag
157

Asp Val Phe Arg Arg Ile Phe Ile Thr Tyr Met Asp Asn Trp Arg Gln

15

20

25

aac aca aca gct gag caa gag gcc ctc caa gcc aaa gtt gat gct gag
205

Asn Thr Thr Ala Glu Gln Glu Ala Leu Gln Ala Lys Val Asp Ala Glu

30

35

40

aac ttc tac tat gtc atc ctg tac ctc atg gtg atg att gga atg ttc
253

Asn Phe Tyr Tyr Val Ile Leu Tyr Leu Met Val Met Ile Gly Met Phe

45

50

55

60

tct ttc atc atc gtg gcc atc ctg gtg agc act gtg aaa tcc aag aga
301

Ser Phe Ile Ile Val Ala Ile Leu Val Ser Thr Val Lys Ser Lys Arg

65

70

75

cgg gaa cac tcc aat gac ccc tac cac cag tac att gta gag gac tgg
349

Arg Glu His Ser Asn Asp Pro Tyr His Gln Tyr Ile Val Glu Asp Trp

80

85

90

cag gaa aag tac aag agc caa atc ttg aat cta gaa gaa tcg aag gcc
397

Gln Glu Lys Tyr Lys Ser Gln Ile Leu Asn Leu Glu Glu Ser Lys Ala

95

100

105

acc atc cat gag aac att ggt gcg gct ggg ttc aaa atg tcc ccc tga
445

Thr Ile His Glu Asn Ile Gly Ala Ala Gly Phe Lys Met Ser Pro

110

115

120

taagggagaa aggcaccaag ctaacatctg acgtccagac atgaagagat gccagtgcca
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cgaggcaaat ccaaattgtc ttgcttaga agaaagtgag ttccttgctc tctgttgaga
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<213> Homo sapiens

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Glu Gln Glu Ala Leu Gln Ala Lys Val Asp Ala Glu Asn Phe Tyr Tyr
 35 40 45

Val Ile Leu Tyr Leu Met Val Met Ile Gly Met Phe Ser Phe Ile Ile
 50 55 60

Val Ala Ile Leu Val Ser Thr Val Lys Ser Lys Arg Arg Glu His Ser
 65 70 75 80

Asn Asp Pro Tyr His Gln Tyr Ile Val Glu Asp Trp Gln Glu Lys Tyr
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Lys Ser Gln Ile Leu Asn Leu Glu Glu Ser Lys Ala Thr Ile His Glu
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Asn Ile Gly Ala Ala Gly Phe Lys Met Ser Pro
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